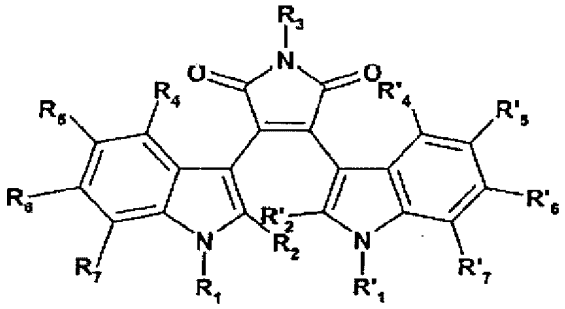
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1. (Currently amended): A method for treating or preventing organ or tissue transplant rejection or an autoimmune disease or for preventing graft-versus-host disease in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of ~~use of~~ a protein kinase C inhibitor of formula I, II, III or IV or a pharmaceutically acceptable salt, hydrate or solvate thereof ~~in the preparation of a pharmaceutical composition for the treatment and prevention of autoimmune diseases~~,

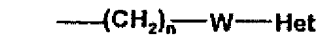
wherein compounds of formula I are



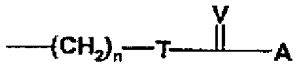
I

wherein

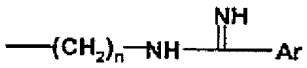
each of R_1 and R'_1, independently, is hydrogen, alkyl, haloalkyl, alkenyl, arylalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, acyl-aminoalkyl, acyloxyalkyl, cyanoalkyl, amidinoalkyl, carboxyalkyl, alkoxycarbonylalkyl, aminocarbonylalkyl, or a group of the formula (a), (b) or (c)



(a)



(b)



(c)

wherein Het signifies a heterocyclyl group; W signifies NH, S or a bond; T signifies NH or S; V signifies 0, S. NH, or NCN; A signifies alkylthio, amino, monoalkylamino or dialkylamino; Ar signifies aryl;

each of R_2 and R'_2, independently, is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, C_1-C_3alkylthio, $S(O)C_1$-C_3alkyl, CF_3;

or R_1 and R_2 form together $—(CH_2)_r—X—CH_2—$ wherein r is 1, 2, or 3, and X is CHR_8 or NR_8 wherein R_8 is $(CH_2)_sR_9$ wherein R_9 is hydrogen, hydroxy, alkoxy, amino,

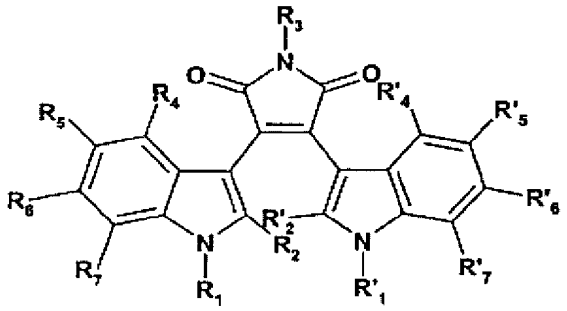
monoalkylamino, dialkylamino, trialkylamino, azido, acylamino, alkoxycarbonyl, cyano, amidino, or aminocarbonyl, and s is 0, 1, 2 or 3;

R_3 is hydrogen or CH_3CO;

each of R_4, R'_4, R_5, R'_5, R_6, R'_6, R_7 and R'_7, independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, —$COO(C_1$-C_3alkyl), CF_3, nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, C_1-C_3alkylthio, or $S(O)C_1$-C_3alkyl; and

n is 1, 2, 3, 4, 5 or 6;

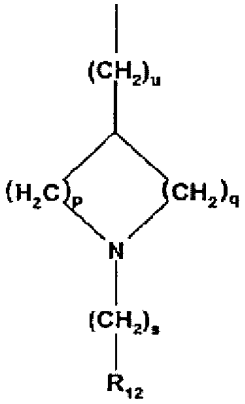
and compounds of formula II are



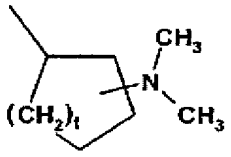
II

wherein

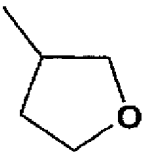
R_1 is a group of formula (d), (e) or (f)



(d)



(e)



(f)

wherein each of p and q independently is 1, 2, 3, or 4;

s is 0, 1,2 or 3;

t is 1 or 2;

u is 0 or 1; and

R_{12} is hydrogen, alkyl, haloalkyl, cycloalkyl, acetyl, aryl, --$CH(aryl)_2$, amino, monoaikylamino, dialkylamino, guanidino, —C(=N(alkoxycarbonyl))NH(alkyoxy-carbonyl), amidino, hydroxy, carboxy, alkoxycarbonyl or heterocyclyl;

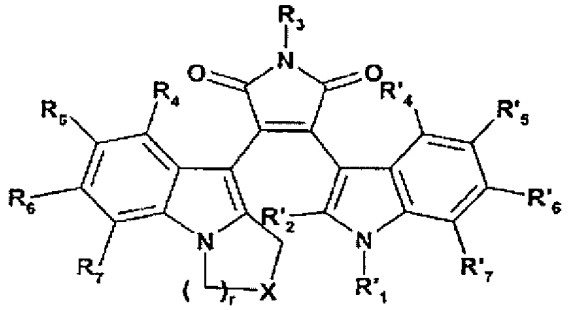
R'_1 is hydrogen, C_{1-4}alkyl, aminoalkyl, monoalkylaminoalkyl, or dialkylaminoalkyl,

each of R_2 and R'_2, independently, is hydrogen, alkyl, alkoxyalkyi, hydroxyalkyl, C_1-C_3alkylthio, $S(O)C_1$-C_3alkyl, CF_3;

R_3 is hydrogen or CH_3CO—; and

each of R_4, R'_4, R_5, R'_5, R_6, R'_6, R_7 and R'_7, independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, --COO(C_1-C_3alkyl), CF_3, nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, C_1-C_3alkylthio, or S(O)C_1-C_3alkyl;

and compounds of formula III are



III

wherein

R'_1 is hydrogen, C_1-C_4alkyl, aminoalkyl, monoalkylaminoalkyl, or dialkylaminoalkyl;

R'_2 is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, C_1-C_3alkylthio, S(O)C_1-C_3alkyl, CF_3

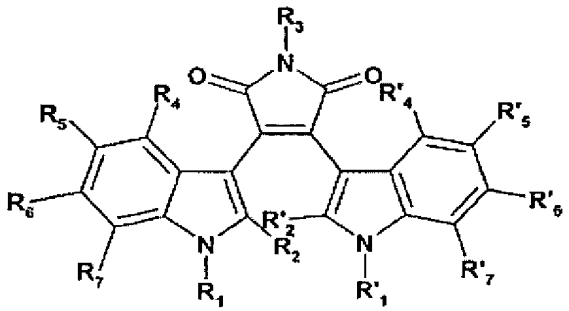
R_3 is hydrogen or CH_3CO—;

each of R_4, R'_4, R_5, R'_5, R_6, R'_6, R_7 and R'_7, independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, —COO(C_1-C_3alkyl), CF_3, nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, C_1-C_3alkylthio, or S(O)C_1-C_3alkyl;

X is CR_8R_9 wherein R_8 is $(CH_2)_sR_{10}$ wherein R_9 is $(CH_2)_sR_{11}$, each of R_{10} and R_{11}, independently, is hydroxy, alkoxy, carboxy, acyloxy, amino, monoalkylamino, dialkylamino, trialkylamino, azido, acylamino, alkoxycarbonyl, cyano, amidino, or aminocarbonyl, and s is 0, 1, 2 or 3; and

r is 1, 2, or 3; and

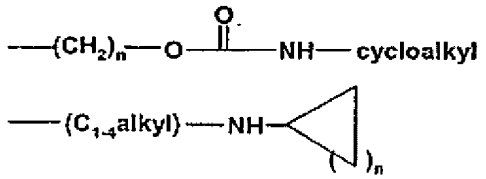
and compounds of formula IV are



IV

wherein

R_1 at is alkylglycose residue or a group of formula (g) or (h)



wherein n is 1, 2, 3, 4, 5 or 6;

R'_1 is hydrogen, C_1-C_4alkyl, cyclopropylmethyl, aminoalkyl, monoalkylaminoalkyl, or, dialkylaminoalkyl;

each of R_2 and R'_2, independently, is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, C_1-C_3alkylthio, S(O)C_1-C_3alkyl, CF_3;

R_3 is hydrogen or CH_3CO—; and

each of R_4, R'_4, R_5, R'_5, R_6, R'_6, R_7 and R'_7, independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, --COO(C_1-C_3alkyl), CF_3, nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, C_1-C_3alkylthio, or S(O)C_1-C_3alkyl.

Claim 2. (Currently amended): ~~Use~~ A method according to claim 1 for the treatment or prevention of an autoimmune disease wherein the autoimmune diseases ~~are~~ is selected from an inflammatory bowel diseases ~~e.g. Crohn's disease and ulcerative colitis;~~ amyotrophic lateral sclerosis; multiple sclerosis; rheumatoid arthritis and hepatitis C.

Claim 3. (Currently amended): ~~Use of a protein kinase C inhibitor of formula I, II, III or IV~~ A method according to claim 1, ~~or a pharmaceutically acceptable salt, hydrate or solvate thereof in the preparation of a pharmaceutical composition~~ for the treatment and prevention of organ or tissue transplant rejection ~~and~~ or for the prevention of graft-versus-host disease.

Claim 4. (Currently amended): ~~Use~~ A method according to claim 1 ~~any one of claims 1 to 3~~ wherein the protein kinase C inhibitor is a compound of formula Ia, Ib, IIa, IIIa or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 5. (Currently amended): ~~Use~~ A method according to claim 1 ~~any one of claims 1 to 3~~ wherein the protein kinase C inhibitor is 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione, or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 6. (Currently amended): A pharmaceutical composition for use in the treatment and prevention of organ or tissue transplant rejection and for the prevention of graft-versus-host disease and/or of autoimmune diseases comprising a protein kinase C inhibitor of formula I, II, III or IV as defined in claim 1 or a pharmaceutically acceptable salt, hydrate or

solvate thereof, together with one or more pharmaceutically acceptable diluents or carriers therefor.

Claim 7. (Currently amended): A composition ~~Composition~~ according to claim 6 wherein the protein kinase C inhibitor is a compound of formula Ia, Ib, IIa, IIIa or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 8. (Currently amended): A composition ~~Composition~~ according to claim 6 wherein the protein kinase C inhibitor is 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 9. (Currently amended): A pharmaceutical combination comprising a) a protein kinase C inhibitor of formula I, II, III or IV as defined in claim 1 , or a pharmaceutically acceptable salt, hydrate or solvate thereof, and b) at least one second agent selected from an immunosuppressant and immunomodulatory drug.

Claim 10. (Currently amended): A pharmaceutical combination comprising a) a protein kinase C inhibitor of formula Ia, Ib, IIa, or IIIa as defined in claim 1, ~~e.g. 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione,~~ or a pharmaceutically acceptable salt, hydrate or solvate thereof and b) at least one second agent selected from an immunosuppressant and immunomodulatory drug.

Claim 11. (Canceled)

Claim 12. (New): A method according to claim 2 wherein the protein kinase C inhibitor is 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione, or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 13. (New): A method according to claim 3 wherein the protein kinase C inhibitor is 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione, or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Claim 14. (New): A pharmaceutical combination according to claim 10 wherein a) is 3-(1-methyl-1H-indol-3-yl)-4-[1-{(1-pyridin-2-ylmethyl)-piperidin-4-yl}-1H-indol-3-yl]-pyrrole-2,5-dione or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione.